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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,760	12/21/2000	Richard Glynne	18547-046600US	4702

33494 7590 07/13/2004

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,760	GLYNNE ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25,26 and 31-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25,31-35,37 and 38* is/are rejected.

7)☒ Claim(s) *26, 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and the response filed on 4/19/04 has been fully considered and entered into the application.

2. Claims 1, 22-24 and 27-30 have been canceled, and new claims 36-38 have been added by the amendment filed on 4/19/04.

3. Claims 25-26 and 31-38 are currently and pending and are being examined in this application.

4. The objection to the specification set forth in the previous office action has been withdrawn in view of the amendment filed on 4/19/04.

5. The new matter rejection of claim 1 set forth in the previous office has been moot in view of the cancellation of claim 1.

6. The rejection of claims 31-33 under 35 U.S.C. 102(b) as being anticipated by Foulkes et al has been withdrawn in view of the amendment and cancellation of claims.

7. The lack of written description rejection of claims 25-26, 31-35 has been withdrawn in view of amendments to the claims and applicants arguments.

8. The art rejection of claims 25-26, 31-35 as being anticipated over WO 97/10365 (LOCKHART et al) and Grosveld et al (US Patent 6,110,666) has been maintained for the reasons of record set forth in the previous office action.

9. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless

the references have been cited by the examiner on form PTO-892, they have not been considered.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 25, 31-35, 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/10365 (LOCKHART et al) and US Patent 6,110,666 (GROSVELD et al).

The instant claims briefly recite a method of screening drug candidates by adding a drug candidate to a B cell that expresses expression profile genes, and determining the effect of the drug candidate on the expression of the expression profile of the gene as compared to a control cell.

Lockhart et al teach methods of monitoring the expression levels of multiplicity genes. The reference teaches a method of identifying genes that are effected by one or more drugs, or

conversely screening a number of drugs to identify those that have effect on particular genes (i.e., see page 8, lines 31-32 and the line bridging pages 8 and 9). The method provides a pool of target nucleic acids from one or more cells (refers to the instant clams steps a) and b)) contacted with the drug or drugs and hybridizing that pool to any of the high-density oligonucleotide arrays. The reference teaches that the expression levels of the genes targeted by the probes in the array are determined and compared to expression levels of genes from control cells not exposed to the drug or drugs (refers to instant claim step d)) (i.e., see page 9, lines 1-6). The genes that are over expressed or under expressed in response to the drugs are identified or conversely the drug or drugs that alter expression of one or more genes is identified (i.e., see page 9, lines 6-8) (refers to instant claim step e). The reference teaches that the genes of particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions (e.g., cancer) and whose expression is thus indicative of the pathological condition. Such genes include but are not limited to HER2 (c-erbB-2/neu), receptor protein kinases associated with etiology of number of tumors including carcinomas of breast, liver, bladder, pancreas as well as glioblastomas, sarcomas, squamous carcinomas, tumor suppressor genes such as p53 and other marker genes such as RAS, MSH2, MLH1, BRCA1. Other genes of particular interest for expression monitoring are genes involved in the immune responses, as well genes involved in cell adhesion and signal transduction, etc. (I.E., see page 8, lines 19-29).

The claimed invention differs from the prior art teachings by reciting B cell that express specific genes (as in the claims). Lockhart et al teaches that the nucleic acid was isolated from the cells, and the cells are not used in the assay method. Lockhart et al teaches a method of identifying genes that are affected by one or more drugs. The reference teaches that the genes of

particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions, and genes involved in immune responses, cell adhesion and signal transduction. The reference does not teach cells that expression of specific gene markers as in the instant claims. However, Grosveld et al (US Patent 6,110,666) teaches pre-B cell possess CD72 (refers to instant claim one expression profile gene of the instant claims) as cellular marker gene (i.e., see column 8, lines 8-9). The reference teaches monitoring the levels of transduction, gene expression and/or the presence or levels of normal encoded protein will assist in selecting and adjusting the dosage administered (i.e., see column 23, lines 34-36).

Thus it would have been obvious to one skilled in the art at the time the invention was made to use the cells that express CD72 gene taught by Grosveld et al in the drug screening methods taught by Lockhart et al, because Lockhart et al teach a method of identifying genes that are effected by one or more drugs, and Lockhart et al teach that the genes of particular interest for expression monitoring include genes involved in pathways associated with various pathological conditions, genes involved in immune response. A person skilled in the art would have been motivated to use the method of monitoring the expression levels of a multiplicity of genes taught by Lockhart et al with different cells, which express the proteins such that the pathological state of the disease is identified.

14. Claims 25, 31-35, and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (US Patent 5,580,722) and Cruse et al (Illustrated Dictionary of Immunology, 1995, pages 56, 59, CRC Press New York).

Foulkes et al disclose a method to determine whether a molecule not previously known to be a modulator of protein biosynthesis is capable of directly and specifically transcriptionally

modulating the expression of a gene encoding a protein of interest associated with treatment of one or more symptoms of a cardiovascular disease (i.e., see abstract). The reference discloses that the cardiovascular disease may be associated with thrombosis (i.e., see column 21). The reference discloses that the protein of interest may be CD36 (i.e., see column 21, line 66) (refers to one of expression profile gene of the instant claims). The reference discloses in claim 1, a method of determining whether a chemical not previously known to be modulator of protein biosynthesis (refers to drug candidate of the instant claims) is capable of modulating expression of a gene encoding a protein of interest, by contacting the sample which contains the predefined eukaryotic cells consisting of gene encoding protein of interest (refers to the cell of the instant claims); quantitatively determining the amount of the signal so produced (refers to step c) of the instant claims); comparing the amount so determined with the amount of produced signal detected in the absence of any chemical being tested refers to instant claim step d)). Foulkes et al do not teach the compound or molecule identified by the claimed method is a potential modulator of B cells or B cell tolerance or potential immunosuppressant. However, the reference teaches the gene encoding the protein of interest is associated with cardiovascular disease and thrombosis and the protein is CD36 (refers to the one of the expression profile gene of the instant claims). CD36 is also known as gp IV or gp IIIb and found on monocytes, macrophages, platelets and on B cells. Thus, the tested molecule is a modulator of a protein interest (CD 36), which is considered as a potential modulator of B cell or immunosuppressant.

The claimed invention differs from the prior art teachings by reciting that the cell used in the claimed method is a B cell, which expresses one or more expression profile genes. Foulkes et al teach a method to determine whether a molecule not previously known to be a modulator of

protein biosynthesis is capable of directly and specifically transcriptionally modulating the expression of a gene encoding a protein of interest. The reference method generally uses eukaryotic cells consisting of gene encoding a protein of interest, and the reference teaches the protein of interest is CD36. Foulkes et al do not teach the use of B cell that expresses one or more expression profile genes. However, it is well known in the art that CD36 is found on B cells (i.e., see the Cruse reference). And further various other genes such as vimentin, CD83, CD73, ApoE, IgD are known to be expressed on B cells (see Cruse). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use different types of cells in the method taught by Foulkes et al. A person skilled in the art would have been motivated to use B cells which express several different genes in the method taught by Foulkes et al to determine the candidate drug candidate such that the disease state is identified.

Allowable Subject Matter

16. Claims 26 and 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

17. Applicant's arguments filed on 4/19/04, regarding the rejection of claims over Grosveld and Lockhart et al, have been fully considered but they are not persuasive.

Applicants argue that there is no discussion in cited references that would enable one of

ordinary skill to identify modulators and neither of the references include any discussion of the genes that are important in B ell tolerance or any other states that B cells can exist.

In response to applicant's argument that 'potential modulator' or 'genes that are important for B cell tolerance', a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., genes that are expressed in a variety of different B cell states or other states of b cell exist) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus the rejections of record have been maintained for the reasons of record.

Conclusion

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PADMASHRI PONNALURI
PRIMARY EXAMINER

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Art Unit 1639